22. The method according to claims 13 or 14, wherein collagenase 3 and MT1-MMP and/or gelatinase A are used as prognostic markers by determination of their mRNA or protein expression, their amount and localisation or their catalytic activity in tissues or body fluids.

23. The method of claim 21, wherein the marker is an HLA antigen or a marker having certain patterns of HLA antigens.--

REMARKS

Specification (Paragraph 1 of Office Action)

The disclosure is objected to because it is allegedly not in proper format. The objection to the disclosure is respectfully traversed. Reconsideration and withdrawal thereof are requested.

The format set forth in Rule 77(b) is not compulsory. Rather, this rule merely sets forth a suggested format rather than a required format. Accordingly, Applicants do not wish to incur the unnecessary expense of rewriting the application. However, several appropriate headings have been incorporated into the text and Applicants have introduced a "Brief Description of the Drawings" section. No new matter has been added. Reconsideration and withdrawal of the objection to the specification in view of Applicants' clarifying and non-limiting amendments to the specification are respectfully requested.

Drawings (Paragraph 2 of Office Action)

The drawing objections are moot in view of the filing of the corrected formal drawings attached hereto.

Claim Rejections Under 35 U.S.C. 112 (Paragraphs 3-8 of Office Action)

Claims 1-12 are rejected by the Examiner under 35 U.S.C. 112, second paragraph, for the reasons set forth in paragraphs 4-8 of the Office Action. These rejections are respectfully traversed. Reconsideration and withdrawal thereof are requested.

The rejections to claims 1-12 are moot in view of the cancellation of these claims.

New claims 13-23 have been added to address the matters raised by the Examiner. For example, independent claims 13 and 14 recite various steps as suggested by the Examiner in paragraph 5 of the Office Action. The dependent claims are presented with antecedent basis for the varying terms, thereby addressing this very minor issue raised by the Examiner in paragraph 6 of the Office Action. Phrases objected to by the Examiner in paragraph 7 of the Office Action have been avoided. For instance, note claims 21 and 23. Finally, claims 21 and 22 further define the markers of the previously recited steps and avoid the issues raised in paragraph 8 of the Office Action.

Rejection of Claims 1, 2 and 12 under 35 U.S.C. 102(b) over Fujimoto et al. (Paragraphs 9 and 10 of the Office Action

Claims 1, 2 and 12 have been rejected by the Examiner under 35 U.S.C. 102(b) as being anticipated by Fujimoto et al. for the reasons set forth in paragraph 10 of the Office Action. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

The Present Invention

The present invention as recited in claim 13 relates to a method for prognosis of progression of rheumatoid arthritis (RA) and for the evaluation of clinical course by detecting collagenase 3 as a prognostic clinical marker, which comprises contacting tissues or body fluids with a substance that is able to bind to collagenase 3 mRNA or to collagenase 3; determining an amount of bounded substance, bounded collagenase 3 mRNA or bounded collagenase 3, and correlating the amount of bounded substance, bounded collagenase 3 mRNA or bounded collagenase 3, with an amount of collagenase 3 in the tissue or body fluid.

The present invention as recited in claim 14 relates to a method for detecting an increased genetic predisposition for rheumatoid arthritis (RA) by detecting collagenase 3 as a prognostic clinical marker, which comprises contacting tissues or body fluids with a substance that is able to bind to

collagenase 3 mRNA or to collagenase 3; determining an amount of bounded substance, bounded collagenase 3 mRNA or bounded collagenase 3, and correlating the amount of bounded substance, bounded collagenase 3 mRNA or bounded collagenase 3, with an amount of collagenase 3 in the tissue or body fluid.

Fujimoto et al.

Fujimoto et al. disclose a method of diagnosis of arthrosis, infiltration and metastasis of cancer and pulmonary fibrosis by determination of free activated MMPs.

Distinctions Between the Present Invention and Fujimoto et al.

First, Fujimoto et al. does not disclose the detection of collagenase 3 as a prognostic clinical marker or the use thereof in the claimed process. Accordingly, the Fujimoto et al. reference cannot destroy the novelty of the present invention.

Second, the Fujimoto et al. reference cannot destroy the novelty of the present invention since the Fujimoto et al. reference does not even disclose rheumatoid arthritis (RA). In this regard, the Examiner should note that arthrosis as disclosed in Fujimoto et al. and the claimed RA are not the same.

Therefore, the Fujimoto et al. reference does not anticipate the present invention for the reasons set forth

above. Thus, the rejection of claims 1, 2 and 12 as applied to new claims 13-23 should be withdrawn by the Examiner.

Rejection of Claims 1-12 Under 35 U.S.C. 103(a) over U.S. Patent 6,143,506 to Golub et al. in view of Wernicke et al. (Paragraphs 11-12 of Office Action

Claims 1-12 have been rejected by the Examiner under 35 U.S.C 103(a) over U.S. Patent 6,143,506 to Golub et al. in view of Wernicke et al. for the reasons set forth in paragraph 12 of the Office Action. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Claims 1-12 are rejected as lacking inventive step over US Patent 6,143,506 to Golub et al. in view of Wernicke et al. Note the discussion in col. 12, lines 27-40 of US Patent 6,143,506 to Golub et al., which recites that MMP-13 is thought to play an important role in the destruction of calcified connective tissues during arthritic an other diseases. Wernicke discloses at page 590, col. 2, paragraph 2 that progressive joint destruction in rheumatic diseases is largely mediated by MMP, mainly synthesized by the synovial lining and cartilage, and that an increase in collagenase expression has been observed in rheumatoid arthritis. The Examiner concludes that it would be obvious to use the diagnostic method of Golub for the diagnosis of destructive joint diseases.

With respect to U.S. patent 6,143,506, the Examiner notes the method for measuring the catalytic activity of the pro-enzyme and the activated enzyme (col. 4, lines 26-36, col. 9, lines 30-34 and col. 16, lines 29-35), and the following portions of Lindy: Abstract, page 1392 (left column, third paragraph; and right column), page 1393 (right column) page 1394 (right paragraph), page 1398 (left column; and Stalhle-Backdahl et al. at page 721 (right column) and page 726 (right column).

Distinctions Between the Present Invention and Golub et al. in View of Wernicke et al.

Briefly, the Examiner's position is that it is obvious to use the diagnostic method as disclosed by Golub et al. for the diagnosis of destructive joint diseases. However, the present invention relates to the use of collagenase 3 as a prognostic marker. A prognosis of progression of rheumatoid arthritis (RA) and the evaluation of clinical course by detecting collagenase 3 in an early phase of the disease makes it possible to start an intensive therapy in sufficient time to prevent the progressive destruction of cartilage. These features of the present invention are nowhere suggested by the combination of prior art relied upon the Examiner. Therefore, reconsideration and withdrawal of the rejection of claims 1-12 as applied to claims 13-23 are respectfully requested.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a one (1) month extension of time for filing a reply in connection with the present application, and the required fee of $55.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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3658-0103P

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

On page 1, the title has been amended as follows:

TITLE: USE OF COLLAGENASE 3 FOR DETECTING DESTRUCTIVE DISEASES OF THE JOINTS, ESPECIALLY FOR PROGNOSING THE PROGRESSION OF THE DISEASE AND THE GENETIC PREDISPOSITION FOR RHEUMATOID ARTHRITIS

The paragraph beginning on page 1, line 1, has been amended as follows:

[Description] BACKGROUND OF THE INVENTION

A paragraph has been added before the paragraph beginning on page 3, line 16 as follows:

BRIEF SUMMARY OF THE INVENTION

A paragraph has been added before the paragraph beginning on page 4, line 14 as follows:

BRIEF DESCRIPTION OF THE DRAWINGS

FIG 1 shows mRNA expression of collagenase 3 in the synovial membrane preparations of patients by Northern Blot analysis;

FIGS 2A and 2B show results of therapy with medicaments in patients with collagenase 3 mRNA expression in the synovial membrane; and

FIG 3 shows rheumatological family anamnesis with regard to RA.

DETAILED DESCRIPTION OF THE INVENTION

The paragraph beginning on page 10, line 1, has been amended as follows:

[Patent Claims] WE CLAIM:

IN THE CLAIMS

Claims 1-12 have been cancelled.

Claims 13-23 have been added.